EXHIBIT A

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COMMONWEALTH OF MASSACHUSETTS

MIDDLESEX, ss.

SUPERIOR COURT DEPARTMENT
OF THE TRIAL COURT
CIVIL ACTION No. 2013-03400-O

IN RE: CONSOLIDATED FRESENIUS CASES

MEMORANDUM OF DECISION AND ORDER ON THE PLAINTIFFS' AND FRESENIUS' MOTIONS PURSUANT TO *DAUBERT* v. *MERRELL DOW PHARMACEUTICALS, INC.*, AND *COMMONWEALTH* v. *LANIGAN*

The Plaintiffs and defendants Fresenius Medical Care Holdings, Inc., Fresenius USA, Inc., Fresenius USA Manufacturing, Inc., Fresenius USA Marketing, Inc., and Fresenius USA Sales, Inc. (collectively, "Fresenius") have moved to exclude certain general causation, FDA regulatory, and specific causation experts from trial or limit their opinions pursuant to Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579 (1993), and Commonwealth v. Lanigan, 419 Mass. 15 (1994). For the following reasons, the parties' motions are **ALLOWED** in part and **DENIED** in part.

BACKGROUND

During hemodialysis, a patient is connected to a hemodialysis machine while his blood is removed from his body. His blood circulates through the dialyzer then back into his body. During this process, waste products are removed from the blood and bicarbonate is added to the blood. The dialyzer contains hollow tubes made of a semi-permeable membrane; surrounding the tubes is dialysate, a liquid solution which consists of purified water, bicarbonate concentrate, and acid concentrate. The patient's doctor prescribes the amount of bicarbonate concentrate for the dialysate; the acid concentrate component of the dialysate is either NaturaLyte, a liquid, or GranuFlo, a powder, both of which Fresenius manufactures. NaturaLyte contains 4

milliequivalents per liter ("mEq/L") of acetate; GranuFlo contains 8 mEq/L of acetate. The liver converts the acetate into bicarbonate.

I. **The Plaintiffs' Position**

As a result of the conversion of acetate into bicarbonate, the patient's serum bicarbonate levels increase, thereby exposing the dialysis patient to a greater amount of serum bicarbonate than the patient's physician anticipated when prescribing the bicarbonate concentrate. Over time, then, the patient develops high levels of serum bicarbonate which lead to metabolic alkalosis, which, in turn, increases the patient's risk of arrhythmia, cardiopulmonary arrest, and sudden cardiac arrest. The sum of bicarbonate that the patient receives from the bicarbonate concentrate and from the acetate conversion is "total buffer." The Plaintiffs allege that Fresenius should have warned physicians to be aware of the total buffer when prescribing the bicarbonate concentrate.

II. **Fresenius' Position**

Fresenius disputes the total buffer theory. Even assuming that the acetate, by metabolizing into bicarbonate, raises the patient's serum bicarbonate level higher than the bicarbonate concentrate prescription, the process of diffusion during dialysis causes the serum bicarbonate to diffuse back into the dialysate. In essence, the patient's post-dialysis serum bicarbonate can never significantly exceed the bicarbonate prescription in the dialysate.

DISCUSSION

In Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579 (1993), the Supreme Court held that the court must conduct "a preliminary assessment of whether the reasoning or methodology underlying the testimony is scientifically valid, and of whether that reasoning or methodology

properly can be applied to the facts in issue." Id. at 592-593. "The Court, emphasizing the need for a flexible inquiry, provided a nonexhaustive list of factors to consider in evaluating the reliability of the expert's testimony, including testing, peer review and publication, error rates, and general acceptance in the relevant scientific community." Palandjian v. Foster, 446 Mass. 100, 106-107 (2006); see Daubert, 509 U.S. at 593-594. In Commonwealth v. Lanigan, 419 Mass. 15 (1994), the Supreme Judicial Court "adopted in part the United States Supreme Court's reasoning in Daubert . . ., and held that 'a proponent of scientific evidence may demonstrate the reliability or validity of the underlying scientific theory or process by some other means, that is, without establishing general acceptance.'" Canavan's Case, 432 Mass. 304, 310 (2000), quoting Lanigan, 419 Mass. at 26; see Salvas v. Wal-Mart Stores, Inc., 452 Mass. 337, 351 n.41 (2008) (relying on Lanigan for proposition that "'some other means,'" may include "satisfying the test set out in Daubert"). Expert testimony may be unreliable where it falls "outside the range where experts might reasonably differ, and where the jury must decide among the conflicting views of different experts, even though the evidence is 'shaky.'" Kumho Tire Co. v. Carmichael, 526 U.S. 137, 153 (1999). "[A] party seeking to introduce scientific evidence may lay an adequate foundation either by establishing general acceptance in the scientific community or by showing that the evidence is reliable or valid through an alternate means." Canavan's Case, 432 Mass. at 310 (citation omitted).

The overarching subject of the court's inquiry "is the scientific validity – and thus the evidentiary relevance and reliability – of the principles that underlie a proposed submission. The focus, of course, must be solely on principles and methodology, not on the conclusion that they generate." Daubert, 509 U.S. at 594-595 (footnote omitted). This "gatekeeping function . . . is

the same regardless of the nature of the methodology used: to determine whether 'the process or theory underlying a scientific expert's opinion lacks reliability [such] that [the] opinion should not reach the trier of fact.'" Canavan's Case, 432 Mass. at 313 (alterations in original), quoting Lanigan, 419 Mass. at 26. For example, "[o]bservation informed by experience is but one scientific technique that is no less susceptible to Lanigan analysis than other types of scientific methodology." Id. at 313. "If the proponent can show that the method of personal observation is either generally accepted by the relevant scientific community or otherwise reliable to support a scientific conclusion relevant to the case, such expert testimony is admissible." Id. at 314.

Conversely, "expert testimony concerning the standard of care generally need not be subject to a Daubert-Lanigan analysis. Such testimony is based on the expert's knowledge of the care provided by other qualified physicians, not on scientific theory or research . . . . [and it is] 'not an opinion derived from data or other scientific inquiry by employing a recognized methodology.'" Palandjian, 446 Mass. at 108 (citation omitted). "The focus, then, is not truly on the 'methodology' underlying the expert's opinion, but on whether the expert's qualifications create a foundation adequate to support the expert's statement of the standard of care." Id. at 108 n.12; see id. at 110 n.15 (noting that "expert's qualifications alone do not necessarily establish the reliability of testimony concerning other specialized knowledge, including increased risk"). Where, however, "the proponent of expert testimony incorporates scientific fact into a statement concerning the standard of care, that science may be the subject of a Daubert-Lanigan inquiry." Id. at 108-109; see, e.g., id. at 109 (noting that expert opinion "about increased risk, like diagnosis and causation, involves the application of science to patient care").

"[T]he burden is on the proponent of expert testimony to demonstrate its reliability, not

on the opposing party to refute it." Id. at 112 n.17. There are aspects of expert testimony, however, that do not require a Daubert-Lanigan analysis. First, "[n]ormally, failure to include variables will affect that analysis' probativeness, not its admissibility.'" Salvas, 452 Mass. at 360 (citation omitted). Second, "any failure to take account of additional factors affects the probativeness, rather than the admissibility, of" the expert's evidence. Id. Third, "failure of [the expert] to account for the factors [that the rebuttal expert] identifies may render his analysis 'less probative than it otherwise might be,' . . . but would not render his analysis inadmissible." Id. (internal citation omitted). Finally, "[v]igorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence." Daubert, 509 U.S. at 596; see id. (characterizing "[t]hese conventional devices" as "appropriate safeguards where the basis of scientific testimony" is relevant and reliable).

FRESENIUS' MOTIONS

I. Fresenius' Motion to Exclude Certain Statements in the Hakim Memo as Well as Plaintiffs' Experts' Opinions Based on those Statements

On November 4, 2011, Fresenius' Medical Office distributed an internal memorandum to medical directors and attending physicians at Fresenius clinics ("Hakim Memo"). Fresenius argues that the Plaintiffs' experts should not be permitted to render opinions based on the Hakim Memo because it serves as an unreliable, unsupported, and speculative foundation. Fresenius points to seven opinions that do not meet the standards for expert testimony:

> 1. "The major cause of metabolic alkalosis in dialysis patients is inappropriately high dialysate total buffer concentration." Hakim Memo (Exhibit 1 to Fresenius' Motion), at 1.
>
> 2. "There are instances whereby the physicians' bicarbonate prescriptions were

kept the same when shifting to power [sic] concentrate (Granuflo [sic]) (failing to account for the additional 8 mEq/L of sodium acetate), thus exposing patients to a higher total buffer load than intended." Hakim Memo (Exhibit 1 to Fresenius' Motion), at 5.

3. "The bicarbonate prescription entered into the dialysis machine underestimates the total buffer that the patient receives from the dialysate – *by ~8 mEq/L in the case of dialysate prepared from Granuflo* [sic] *(powder) or by ~4 mEq/L in the case of dialysate prepared from NaturaLyte (liquid)* – since acetate is rapidly converted into bicarbonate by the liver." Hakim Memo (Exhibit 1 to Fresenius' Motion), at 1-2 (emphasis in original).

4. "Over time, the progressive shift towards higher ***pre-dialysis*** serum bicarbonate levels not only implies that more patients have alkalosis prior to dialysis, but that an even higher percentage of patients have alkalosis post-dialysis." Hakim Memo (Exhibit 1 to Fresenius' Motion), at 1 (emphasis in original).

5. "The KDOQI [i.e., Kidney Disease Outcome Quality Initiative] guidelines focused on correction of acidosis, so it was not surprising that pre-dialysis bicarbonate levels have increased over time, from 22.9±3.1 mEq/L in the 2004 [Fresenius] prevalent [hemodialysis] patient study, to 24.1±3.5 mEq/L for September, 2011 (median 24.0 mEq/L), with 25% of patients at ≥26.0 mEq/L, 15% with ≥28.0 mEq/L and ~3% with ≥30.0 mEq/L – shown in Figure 1, below." Hakim Memo (Exhibit 1 to Fresenius' Motion), at 2 (footnote omitted).

6. "Over time, there has been a shift towards higher dialysate bicarbonate prescriptions accompanied by increasing serum bicarbonate levels before dialysis and presumably much higher post dialysis. This issue needs to be addressed urgently." Hakim Memo (Exhibit 1 to Fresenius' Motion), at 5.

7. "The current analysis determined that: '*borderline elevated pre-dialysis bicarbonate levels and overt alkalosis are significantly associated with 6 to 8 fold greater risk of CP arrest and sudden cardiac death in the dialysis facility.*'" Hakim Memo (Exhibit 1 to Fresenius' Motion), at 1 (italics and internal quotations in original).

Fresenius' motion is **ALLOWED** because there are too many shortcomings in the support for the challenged findings to allow them to serve as a basis of other expert opinions.

A. Relevant Background

Guideline #14 of the Kidney Disease Outcome Quality Initiative, or KDOQI, guidelines that were released in June 2000, states that "[p]redialysis or stabilized serum bicarbonate levels should be maintained at or above 22 [mEq/L]." KDOQI Guidelines (Exhibit 7 to Fresenius' Motion), at FMC-MDL-00020678. In December 2000, Fresenius' chief medical director at the time, Dr. J. Michael Lazarus ("Dr. Lazarus") issued an internal memorandum to Fresenius medical directors discussing the KDOQI guidelines, and stating that "low pre-dialysis levels seem to be a greater problem than [he] expected . . . ." December 2000 Memorandum (Exhibit 15 to Fresenius' Motion), at 1. After evaluating laboratory results, he discovered that "[a]pproximately 58% of [Fresenius] patients are below the recommended level of 22 [mEq/L]." December 2000 Memorandum (Exhibit 15 to Fresenius' Motion), at 2.

As a result, he urged the medical directors to review each patient's bicarbonate levels, December 2000 Memorandum (Exhibit 15 to Fresenius' Motion), at 9, and, through subsequent internal memoranda, instructed them that by raising the prescribed amount of bicarbonate concentrate, they could raise patients' serum bicarbonate levels. March 2001 Memorandum (Exhibit 24 to Fresenius' Motion), at 4 ("Observe and monitor the patient's serum bicarbonate level to determine that the prescribed dialysate bicarbonate is actually being delivered . . . . If not, the physician should establish a new bicarbonate prescription . . . ." (underlining in original)); April 2002 Memorandum (Exhibit 13 to Fresenius' Motion), at FMC-MDL-00025598 (reiterating that patients with pre-dialysis serum bicarbonate levels below 22 mEq/L "should appropriately receive higher bicarbonate dialysate" and patients with pre-dialysis levels above 28-30 mEq/L "should receive a lower dialysate bicarbonate concentration"); July 2005

Memorandum (Exhibit 50 to Fresenius' Motion), at 3 ("[I]t is important to understand and prescribe a dialysate bicarbonate concentration which, in combination with the acetate in the acid concentrate, delivers the desired total buffer.").

The Dialysis Outcomes and Practice Patterns Study ("DOPPS 1"), issued in 2004, analyzed the question of whether "associations exist between predialysis serum bicarbonate concentrations . . . and mortality among [hemodialysis] patients." DOPPS 1 (Exhibit 33 to Fresenius' Motion), at FMC-MDL-00023050. DOPPS 1 concluded, in part, that "[a] significantly increased risk for mortality and hospitalization . . . is observed for patients with very high midweek predialysis serum bicarbonate levels (>27 mEq/L . . .) who are dialyzed thrice weekly." DOPPS 1 (Exhibit 33 to Fresenius' Motion), at FMC-MDL-00023058; see DOPPS 1 (Exhibit 33 to Fresenius' Motion), at FMC-MDL-00023053 (explaining that adjusting for certain factors caused relative risk "associated with alkalosis [to become] less pronounced and nonsignificant whereas the [relative risk] associated with midweek predialysis acidosis increased and became significant for all bicarbonate levels of 17.0 mEq/L . . . or less"). In July 2005, Dr. Lazarus issued an internal memorandum to Fresenius medical directors referencing DOPPS 1 and noting its conclusion that, "as in [Fresenius'] study, there is no increased hazard risk between 24 and 28 [mEq/L] of serum bicarbonate." July 2005 Memorandum (Exhibit 50 to Fresenius' Motion), at 3; see July 2005 Memorandum (Exhibit 50 to Fresenius' Motion), at 4 (chart showing "total buffer" is sum of bicarbonate prescription and acetate contribution).

Meanwhile, Dr. Raymond Hakim ("Dr. Hakim"), the chief medical officer of a Fresenius competitor, noted that pre-dialysis serum bicarbonate levels in patients "have been rising steadily . . . . suggest[ing] a much higher level of alkalosis after dialysis and should be of concern . . . ."

February 2005 Email (Exhibit 64 to Fresenius' Motion), at FMC-MDL-00022889. He recommended that his medical staff "[u]se dialysate with TOTAL bicarbonate levels NOT to exceed 35 meq/L; total bicarbonate includes both the acetate and bicarbonate moieties." Id. (capitalization in original). Dr. Hakim explained that his "concern is not about the level of bicarb[onate] of 24-25 [mEq/L], but of the levels immediately post-dialysis when it is 45-50 meq/L." September 2005 Email (Exhibit 37), at FMC-MDL-00027948.

Dr. Hakim began working for Fresenius in 2006 after Fresenius acquired Dr. Hakim's employer. Dr. Lazarus retired in 2010, and Dr. Hakim became Fresenius' chief medical officer. Dr. Hakim commissioned Fresenius' epidemiologist Dr. Eduardo Lacson ("Dr. Lacson") to study the serum bicarbonate levels of Fresenius' dialysis patients who suffered cardiopulmonary arrest in Fresenius clinics in 2010, in order to determine whether there was an association between high serum bicarbonate levels and increased risk of cardiopulmonary arrest ("2010 Study"). The Hakim Memo purports to set forth the results of this 2010 Study.[1]

B. "The major cause of metabolic alkalosis in dialysis patients is inappropriately high dialysate total buffer concentration" and "There are instances whereby the physicians' bicarbonate prescriptions were kept the same when shifting to power [sic] concentrate (Granuflo [sic]) (failing to account for the additional 8 mEq/L of sodium acetate), thus exposing patients to a higher total buffer load than intended."

These conclusory statements reveal nothing about the methodology behind them, thus

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[1]Although others within Fresenius reviewed the Hakim Memo before its dissemination, this review was not "peer review" in the sense that Daubert contemplates. "[S]ubmission to the scrutiny of the scientific community is a component of 'good science,' in part because it increases the likelihood that substantive flaws in methodology will be detected." Daubert, 509 U.S. at 593. The court "must not define the 'relevant scientific community' so narrowly that the expert's opinion will inevitably be considered generally accepted." Canavan's Case, 432 Mass. at 314 n.6. Rather, the "relevant scientific community must be defined broadly enough to include a sufficiently broad sample of scientists so that the possibility of disagreement exists." Id. Here, that "broad sample" extends beyond the Fresenius community.

rendering them mere ipse dixit with no data supporting or explaining them. See General Electric Co. v. Joiner, 522 U.S. 136, 146 (1997) (holding that where "opinion evidence . . . is connected to existing data only by the ipse dixit of the expert[,] [a] court may conclude that there is simply too great an analytical gap between the data and the opinion proffered"); Daubert, 509 U.S. at 595 (footnote omitted) ("The focus, of course, must be solely on principles and methodology, not on the conclusion that they generate."). Significantly, the terms "inappropriately high" or "higher total buffer load" are not defined, and relatedly, the absence of any data on which the conclusions are based precludes the conclusions from being tested. See Daubert, 509 U.S. at 593.

C. "The bicarbonate prescription entered into the dialysis machine underestimates the total buffer that the patient receives from the dialysate – *by ~8 mEq/L in the case of dialysate prepared from Granuflo* [sic] *(powder) or by ~4 mEq/L in the case of dialysate prepared from NaturaLyte (liquid)* – since acetate is rapidly converted into bicarbonate by the liver." (Emphasis in original).

This finding stands for the proposition that the dialysis machine does not take into consideration the conversion of acetate into bicarbonate, thereby underestimating the patient's total buffer. Fresenius does not dispute that "acetate is rapidly converted into bicarbonate by the liver." It argues, however, that the balance of this finding is based on that fact without any data supporting the conclusion, without disclosing the methodology by which the conclusion was reached, and without taking into consideration the concentration gradient which occurs during dialysis. See Canavan's Case, 432 Mass. at 313 ("The gatekeeping function pursuant to Lanigan[, 419 Mass. at 26] is the same regardless of the nature of the methodology used: to determine whether 'the process or theory underlying a scientific expert's opinion lacks reliability [such] that [the] opinion should not reach the trier of fact.'"). As a result, the conclusion cannot

be tested or replicated.

D. Increase in Patient Pre-Dialysis and Post-Dialysis Bicarbonate Levels

Fresenius takes the next three findings together as they all stand for the same proposition, i.e., that there has been an increase in patients' pre-dialysis and post-dialysis serum bicarbonate levels. First, this finding is rendered with no supporting data or analysis. Second, the existing data, of which Dr. Hakim was aware, does not support the conclusion that a there was a "progressive shift" to higher pre-dialysis serum levels among Fresenius patients. Specifically:

- Fresenius' 2004 study of its patient population shows a pre-dialysis serum bicarbonate level of 23.68 mEq/L, and a post-dialysis serum bicarbonate level of 28.75 mEq/L. Exhibit 10 to Fresenius' Motion, at 1-2.

- As of 2005, Fresenius' patients' mean pre-dialysis serum bicarbonate levels were approximately 24 mEq/L. Exhibit 9 to Fresenius' Motion, at 28.

- The data from a three-month period ending January 31, 2007, showed levels similar to those from the 2004 study. See Exhibit 8 to Fresenius' Motion.

- A study of data from October 2007 showed an average post-dialysis serum bicarbonate level of 28.61 mEq/L. Norma Ofsthun, Ph.D., Rebuttal Expert Report (Exhibit 88 to Fresenius' Motion), at 10; see November 2007 Email from Dr. Lazarus to Dr. Hakim, et al. (Exhibit 42 to Fresenius' Motion) ("[T]he difference between the pre[-dialysis] and post[-dialysis] [serum bicarbonate] values are exactly as they were when we measured them before several years ago . . . .").

- Finally, in a May 2010 analysis that Dr. Hakim himself commissioned, the median post-dialysis serum bicarbonate levels of Fresenius patients was 28.83 mEq/L. Norma Ofsthun, Ph.D., Rebuttal Expert Report (Exhibit 88 to Fresenius' Motion), at 11.

This data demonstrates that Fresenius' patients' pre-dialysis and post-dialysis serum bicarbonate levels did not undergo a "shift," progressive or otherwise, towards higher levels and pre-dialysis bicarbonate levels have not "increased over time". See Norma Ofsthun, Ph.D., Rebuttal Expert Report (Exhibit 88 to Fresenius' Motion), at 12.

"Experts must provide reasonable bases for their assumptions and inferences, but need not always provide exhaustive explanations of each and every step of their analysis." Zeolla v. Ford Motor Co., 2013 WL 308968, *9 (D. Mass. Jan. 24, 2013). Additionally, this situation is not one where the expert failed to include certain variables or failed to take into account certain factors. See Salvas, 452 Mass. at 360. Here, the Hakim Memo disregards the above-detailed data and fails to provide any basis for its conclusion that the opposite is true, i.e., that pre-dialysis and post-dialysis serum bicarbonate levels increased in Fresenius patients. See Zeolla, 2013 WL 308968, at *9 ("[E]xperts cannot . . . disregard available data."). Without any analysis or explanation as to the methodology used, the conclusion as to this progressive shift is based solely on the ipse dixit of the Hakim Memo's author.

E. "The current analysis determined that: '*borderline elevated pre-dialysis bicarbonate levels and overt alkalosis are significantly associated with 6 to 8 fold greater risk of CP arrest and sudden cardiac death in the dialysis facility*'." (Italics and internal quotations in original).

Fresenius argues that this finding has no support in the presented analysis. First, a portion of this finding is in quotation marks, but the Hakim Memo provides no citation for this quotation. Second, the phrase "'borderline elevated pre-dialysis bicarbonate levels'" is not defined. Third, Figure 2 of the Hakim Memo purports to graph the "Relative Risk of [Cardiopulmonary] Arrest: Bicarbonate." Hakim Memo (Exhibit 1 to Fresenius' Motion), at 3. The "'6 to 8 fold greater risk[,]'" however, is not reflected in this graph; in fact, the highest unadjusted odds ratio estimate is below 6.5. Id. Whatever the methodology Dr. Hakim used to reach the conclusion set forth in this finding, he failed to explain the disconnect between the finding and Figure 2. Fourth, even the Plaintiffs' experts were unable to interpret Figure 2's reference to "% of patients" because of the lack of data or information about methodology in the

Hakim Memo. See Fresenius' Motion, at 53.[2] Finally, the finding appears to equate sudden cardiac arrest and cardiopulmonary arrest without any explanation as to either term.

F. Conclusion

In sum, the findings in the Hakim Memo are conclusory statements that are either not supported by data or are contradicted by certain data of which Dr. Hakim was aware. These findings are therefore not scientifically sound support for the general causation argument, and cannot be used to prove general causation; moreover, the Plaintiffs' experts cannot rely on them.[3] Accordingly, Fresenius' motion is **ALLOWED**.

II. **Fresenius' Motion to Limit the Opinions and Testimony of Dr. Steven Borkan**

Dr. Steven C. Borkan ("Dr. Borkan") is a nephrologist whom the Plaintiffs have named as a expert in general causation. Fresenius asks the court to preclude Dr. Borkan from testifying at trial to three opinions contained within Dr. Borkan's report.[4]

A. First Opinion

In his report, Dr. Borkan states, "Given our understanding of the intimate relationship between bicarbonate and other critical electrolytes at the time acetate- and di-acetate/bicarbonate solutions were introduced, the increase in peri-dialysis deaths due to exposure to excess acetate is both predictable and avoidable." Dr. Borkan Report (Exhibit 3 to Fresenius' Motion), at 22.

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[2]This point concerns Figure 3 of the Hakim Memo as well. Hakim Memo (Exhibit 1 to Fresenius' Motion), at 4.

[3]The admissibility of the Hakim Memo on other grounds is subject to separate motions in limine.

[4]Fresenius' argument that Dr. Borkan's opinion is inadmissible because he relies on the Hakim Memo is moot given this court's decision, above, as to the admissibility of that document. Further, Dr. Borkan's inability to rely on the Hakim Memo does not affect the admissibility of his testimony as he relies on other sources.

1. *Prior Testimony*

Fresenius argues that Dr. Borkan should not be permitted to testify that 4 mEq/L of acetate is "excess" as he has previously testified in the context of other litigation that 4 mEq/L of acetate is acceptable, and that patients at his own clinic are treated with an acid concentrate containing 4 mEq/L of acetate. Any criticism Fresenius has of Dr. Borkan's opinion concerns its weight, not its admissibility.

At his deposition, Dr. Borkan testified that, by "excess" he means "more than what [he] prescribed." Dr. Borkan Deposition (Exhibit 4 to Plaintiffs' Opposition), at 52-53. He further testified that he is

> "concerned that even 4 [mEq/L] could in some cases deliver more bicarbonate than [he] intended . . . . As a result of educating [himself] through the last year, if a patient on dialysis were to complain to [him] of nausea or cramping or feeling poorly, or were to have unexplained hypotension on dialysis, [he] would now include an analysis of [that patient's] acetate into the equation of [his] differential diagnosis, and [he] might consider decreasing the amount of acetate exposure either because [he] was concerned about the excess bicarbonate delivery above [his] prescribed bicarbonate, or because of acetate toxicity. . . . [He] [has] paid more careful attention to the pre-dialysis bicarbonate and decreased bicarbonate exposure to prevent [his] patients from having excess bicarbonate delivery, and that is the most common way [he has] incorporated what [he has] learned in the last year into [his] practice."

Dr. Borkan Deposition (Exhibit 4 to Plaintiffs' Opposition), at 51-52.

With this testimony, more recent in time than Dr. Borkan's previous testimony to which Fresenius refers, see Fresenius' Motion, at 5-7, Dr. Borkan explains that his research has revealed to him the alleged dangers that increased bicarbonate delivery may cause. This "change" in his understanding of this phenomenon concerns the weight of his testimony, not the admissibility. Moreover, throughout his report, Dr. Borkan references various journal articles as support for his opinion that "excess acetate" results in excess bicarbonate, which, in turn, may

result in "peri-dialysis deaths . . . ." Dr. Borkan Report (Exhibit 3 to Fresenius' Motion), at 22; see, e.g., Dr. Borkan Report (Exhibit 3 to Fresenius' Motion), at 23-24. Fresenius' motion is accordingly **DENIED** on this basis.

2. *2.4 mEq/L of Acetate*

Fresenius also seeks to exclude testimony from Dr. Borkan that "excess acetate" is any amount over 2.4 milliequivalents per liter ("mEq/L"). At his deposition, Dr. Borkan testified,

> "A. My understanding is that anything above 2.4 [mEq/L] of acid would enhance bicarbonate delivery, but was not absolutely necessary to maintain the pH of the dialysis solution in a safe range, or to prevent bicarbonate precipitating as calcium carbonate.
>
> . . . .
>
> Q. And so . . . anything above 2.4 [mEq/L] of acid was there to enhance the bicarbonate delivery?
>
> A. I take that from the range of acid that has been traditionally incorporated into dialysis solutions. And when I looked back in the last year as to the range of acid, the lowest I found was 2.4 [mEq/L]. And since those solutions were used, I made the logical conclusion that that was sufficient to maintain the pH parameters of the dialysate and to prevent bicarbonate from precipitating as calcium carbonate. . . .
>
> Q. So your understanding that all that was needed was 2.4 [mEq/L] of acid came from your . . . review of what was available out there as far as acid concentrates are concerned?
>
> A. That's correct."

Dr. Borkan Deposition (Exhibit 4 to Plaintiffs' Opposition), at 90-92. This testimony indicates that Dr. Borkan bases his opinion concerning 2.4 mEq/L of acetate on the fact that the lowest amount of acetate available on the market is 2.4 mEq/L.

At the hearing on this motion, Plaintiffs' counsel stated that Dr. Borkan is "not going to say 2.5 [mEq/L] is automatically worse than 2.4. That's not what he's going to say. And if [the

court] want[s] to restrict him from saying anything in excess of 2.4 [mEq/L] is not accurate because you don't have any data . . . . [T]here are no such products . . . that are 2.5 to 3.9 so obviously no data exists on 2.5 to 3.9. . . . So, asking him to opine on 2.5 to 3.9, that's fallacious." Hearing Transcript (10/14/2015), at 170. Further, Plaintiffs' counsel "argue[d] that [Dr. Borkan's] opinions on NaturaLyte and GranuFlo are still valid, with the exception of him being stricken or restricted from using that specific language with respect to that 2.4 [mEq/L] being automatically safer." Hearing Transcript (10/14/2015), at 177-178.

The court concludes that Dr. Borkan cannot testify that an amount of acetate over 2.4 mEq/L is "excess" because, as Plaintiffs' counsel conceded, no data exists to that effect. Dr. Borkan may, however, testify that the greater the amount of acetate, the greater the potential impact on a patient's serum bicarbonate.

B. Second Opinion

In his report, Dr. Borkan discusses the KDOQI guidelines that were assembled in 2009 "by the American Kidney Foundation, establish[ing] a target pre-dialysis bicarbonate level of 20-22 mEq/L . . . with 24 mEq/L being the normal value. Subsequent guidelines provided by [another organization] continue to support a bicarbonate level of 20-22 mEq/L in patients with chronic kidney disease . . . ." Dr. Borkan Report (Exhibit 3 to Fresenius' Motion), at 15; see Dr. Borkan Deposition (Exhibit 4 to Plaintiffs' Opposition), at 23 ("I try to keep my dialysis patients between 22 and 24 [mEq/L] of bicarbonate pre-dialysis . . . ."). Fresenius seeks to preclude Dr. Borkan from opining that Fresenius "increased the risk of" cardiopulmonary arrest by "[e]xposing all dialysis patients including those with low or high pre-dialysis bicarbonate levels to acetate or di-acetate [i.e., NaturaLyte or GranuFlo]; these patients are predicated to be a

higher risk for life-threatening consequences than those with bicarbonate levels closer to the pre-dialysis target range." Dr. Borkan Report (Exhibit 3 to Fresenius' Motion), at 41. Fresenius argues that, of all of the plaintiffs involved in this consolidated matter, more than a quarter of them fall within the "target" pre-dialysis bicarbonate level of 22-24 mEq/L, thus Dr. Borkan's opinion does not "fit" these cases.

The "central thesis" of Dr. Borkan's report, and, thus, his opinion as to general causation, "is that hemodialysis using acetate or di-acetate baths, in conjunction with the high bicarbonate containing dialysate solutions . . . represent an acute and failed experiment unparalleled in human physiology." Dr. Borkan Report (Exhibit 3 to Fresenius' Motion), at 3. Further, "the addition of acetate or di-acetate to bicarbonate containing dialysis solutions[] altered a critical medical device used for [dialysis] (the dialysate), predisposed vulnerable patients to death without their knowledge and without a standardized or timely mechanism for adjusting the bicarbonate delivered to maintain patients at a safe pre-hemodialysis bicarbonate level recommended by the prevailing KDOQI Guidelines." Dr. Borkan Report (Exhibit 3 to Fresenius' Motion), at 23. Within the context of these general causation opinions, Dr. Borkan's opinions as to the "target" pre-dialysis bicarbonate level concerns the weight of his testimony rather than the admissibility. Moreover, as the Plaintiffs point out, Fresenius' argument conflates general and specific causation, and is not the basis for exclusion under Daubert.

Fresenius' motion to preclude Dr. Borkan from rendering this testimony is **DENIED**.

C. Third Opinion

Finally, Dr. Borkan states that Fresenius "increased the risk of" cardiopulmonary arrest by "[f]ailing to study the rate of acetate-to-bicarbonate conversion in both normal and patients

with slower or faster conversion rates; the rate of acetate-to-bicarbonate conversion is important for determining when the blood bicarbonate level 'spikes' in dialysis patients; the timing of the spike is a key determinant of the toxic effects of acute metabolic alkalosis including [cardiopulmonary arrest] and death both during and after the procedure." Dr. Borkan Report (Exhibit 3 to Fresenius' Motion), at 41, 42. Fresenius argues that Dr. Borkan has not assigned a time frame to this "spike," thus rendering his opinion vague and contrary to the scientific literature which establishes that there is no evidence of acetate metabolism more than four hours after dialysis.[5] Therefore, Fresenius argues, the court should preclude Dr. Borkan from testifying that a "spike" in a patient's post-dialysis serum bicarbonate resulting from acetate metabolism can occur more than four hours after the patient has completed his dialysis session.

The Plaintiffs argue that "[w]hen Dr. Borkan is referring to a 'spike,' Dr. Borkan is referring to what happens immediately as a result of the infusion of acetate into the body." Hearing Transcript (10/14/2015), at 151; Hearing Transcript (10/14/2015), at 177 (arguing that "spike" to which Dr. Borkan refers is the "run-up at the beginning of dialysis"). In his report and deposition testimony, however, Dr. Borkan opines that a spike in serum bicarbonate may occur during dialysis or after dialysis. First, Dr. Borkan writes earlier in his report:

> "Assuming that the blood and dialysate bicarbonate levels are nearly in steady state . . ., the addition of [NaturaLyte or GranuFlo] would add to the bicarbonate in the bloodstream at a rate equivalent to the transfer rate of acetate from the dialysate in the blood. Rapid conversion of this acetate to bicarbonate would further increase the patient's bicarbonate level, resulting in an even larger *spike* in the bicarbonate level and more severe metabolic alkalosis than anticipated by the [n]ephrologist. Only after the *spike* in bicarbonate would bicarbonate slowly begin to diffuse into the dialysate while the rapid conversion of acetate into

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[5]The Plaintiffs dispute that the scientific literature supports the view that there is a four-hour post-dialysis "risk window." See Plaintiffs' Opposition, at 28-29 & nn.33-34.

> bicarbonate by the liver continued to facilitate acetate diffusion into the blood from the dialysate. Together, these two processes . . . would more likely than not cause higher than prescribed blood bicarbonate levels."

Dr. Borkan Report (Exhibit 3 to Fresenius' Motion), at 24 (internal citations omitted) (emphasis added). In this instance, the "spike" occurs during dialysis.

Second, Dr. Borkan uses the word "spike" to refer to the period after dialysis, writing that

> "a doubling of the acetate content (from 4 mEq/L acetate to 8 mEq/L di-acetate) in the dialysate doubles the amount available for conversion to bicarbonate in the blood stream. The rapidity of converting acetate to bicarbonate depends upon several factors that include liver metabolism, liver perfusion, muscle mass, and other factors . . . . These factors, acting alone or together, are highly likely to slow acetate metabolism and *delay the 'bicarbonate spike' until after dialysis is completed*."

Dr. Borkan Report (Exhibit 3 to Fresenius' Motion), at 29 (emphasis added). At his deposition, Dr. Borkan appears to describe the same events substituting the word "peak" for "spike," testifying that he "would expect that either at the end of dialysis or in the hours after dialysis, depending upon the rate of acetate to bicarbonate conversion, that *the patient's serum bicarbonate level would peak,* but the timing of the peak could differ. . . . Assuming that the patient metabolizes the acetate completely to bicarbonate, the average patient would accomplish that within hours after dialysis." Dr. Borkan Deposition (Exhibit 4 to Plaintiffs' Opposition), at 78-79 (emphasis added); see Dr. Borkan Report (Exhibit 3 to Fresenius' Motion), at 19.

In both his report and deposition testimony, Dr. Borkan references the "Graham study" from 2001, involving "nine patients dialyzed for 4 hours against a 35 mEq/L HCO_3 bath . . . ." Dr. Borkan Report (Exhibit 3 to Fresenius' Motion), at 20. The serum bicarbonate levels of two patients "remained elevated despite 44 [hour] follow up . . . . [and] two patients also experienced bicarbonate 'spikes' several hours after dialysis was completed . . . ." Id. At his deposition, he

explained that, from the Graham study, "not only do we not know precisely when the bicarbonate could peak in the individual patient, and we don't know precisely what the range is of acetate to bicarbonate conversion, there are probably a subset of patients who we send home from the dialysis unit with substantial metabolic alkalosis that persists for as long as until the next dialysis session [i.e., forty-eight hours later]." Dr. Borkan Deposition (Exhibit 4 to Plaintiffs' Opposition), at 80. Dr. Borkan, then, apparently relies on the Graham study for the time frame in which a "spike" may occur.[6]

Any challenge to these opinions concerns the weight of Dr. Borkan's testimony, not its admissibility. Fresenius' motion is **DENIED** on this basis.

III. **Fresenius' Motion to Limit the Opinions and Testimony of Plaintiffs' Four FDA Regulatory Experts**

The Plaintiffs offer four experts (collectively, "Regulatory Experts") to testify about medical device industry practice and custom: Peggy Pence, Ph.D. ("Dr. Pence"); Timothy A. Ulatowski ("Ulatowski"); George M. Samaras, Ph.D. ("Dr. Samaras"); and Bruce H. Barkalow, Ph.D. ("Dr. Barkalow"). Fresenius argues that the Regulatory Experts render opinions outside their areas of expertise, reach improper legal conclusions, and make statements about Fresenius' knowledge and state of mind. See Appendices A-E to Fresenius' Motion (identifying portions of Regulatory Experts' reports that court should exclude).

At the hearing, counsel for Fresenius indicated that certain arguments in its motion "have

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[6]It appears that Dr. Borkan does assign a time from within which the spike in serum bicarbonate may occur. Regardless, Fresenius' argument that this testimony contradicts his testimony in different litigation is an issue that goes to the weight of Dr. Borkan's testimony. See Exhibit 2 to Fresenius' Motion, at 260-261 (testifying that there is "a *defined period* when it would be biochemically feasible to ascribe the untoward event to that spike in bicarbonate caused by GranuFlo exposure" (emphasis added)).

been mooted largely by agreement of the parties and will be handled, if at all, in the motion in limine practice." Hearing Transcript (10/15/2015), at 88-89; see Hearing Transcript (10/15/2015), at 113 (listing Fresenius' arguments that have been resolved or left for motion in limine practice). The only arguments before the court, then, are Fresenius' arguments (A) that the Regulatory Experts should be precluded from testifying about matters outside their areas of expertise; (B) that the Regulatory Experts should be precluded from offering legal opinions; and (C) that the Regulatory Experts should be precluded from offering narratives and elaborations of Fresenius' documents. The Plaintiffs concede in their opposition that Regulatory Experts "will not testify to anyone's state of mind, they will not offer legal opinions, they will not speculate, and they will not simply read documents into the record devoid of analysis." Plaintiffs' Opposition, at 1.

A. Expertise

"'An expert witness may give testimony "on matters within the witness's field of expertise [and this testimony] is admissible whenever it will aid the jury in reaching a decision, even if the expert's opinion touches on the ultimate issues that the jury must decide."'" Peterson v. Foley, 77 Mass. App. Ct. 348, 356 (2010) (citations and internal quotation omitted) (alteration in original); Foreign Car Ctr., Inc. v. Salem Suede, Inc., 40 Mass. App. Ct. 15, 21 (1996). A witness is qualified if he "'possesses sufficient skill, knowledge or experience in the field of his testimony that the jury may receive appreciable assistance from it.'" Peterson, 77 Mass. App. Ct. at 350 (citations omitted).

The Regulatory Experts are certainly qualified to testify to the regulatory requirements for medical device manufacturers: Dr. Pence is a toxicologist who owns a consulting firm that,

inter alia, provides product development services to medical device companies; Ulatowski is a biomedical engineer who serves as a regulatory consultant to the medical device industry; Dr. Samaras has doctorates in physiology, engineering management, and industrial/organizational psychology, worked for the FDA for two years, and currently owns a consulting firm that provides, in part, regulatory consulting; and Dr. Barkalow is a biomedical engineer who owns a consulting firm that provides biomedical engineering consulting services for medical device companies. Fresenius argues that the Regulatory Experts are not qualified to testify about acid-based chemistry, the effects of GranuFlo and NaturaLyte on patient serum bicarbonate levels, and the health risks allegedly posed to patients treated with GranuFlo and NaturaLyte. With this testimony, Fresenius asserts, the Regulatory Experts render opinions approaching causation which they base solely on their reliance on Fresenius' internal documents.

This court agrees that the Regulatory Experts are not general causation experts – nor do they purport to be – and are therefore not qualified to offer opinions about the risks created by actions or inactions. See Peterson, 77 Mass. App. Ct. at 354 ("As observed in a slightly different context, 'nothing in either Daubert . . . or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the ipse dixit of the expert.'" (alteration omitted)). Plaintiffs' counsel conceded as much at the hearing on this motion, assuming the court ruled in this manner: "If that's the court's ruling, ... [the Regulatory Experts] would explain . . . what the industry standards are and how medical device companies operate and why they look at risks, why they identify risks, why they control risk and how they go about doing that without linking it to the causation opinions . . . ." Hearing Transcript (10/15/2015), at 101. The Regulatory Experts may, however, be "ask[ed] if they reviewed a set

of documents or records and whether there was evidence of X [i.e., action] or evidence of not X [i.e., inaction]. . . ." Hearing Transcript (10/15/2015), at 117.

B. Legal Opinions

Fresenius also argues that the Regulatory Experts cannot make legal conclusions. The end result is similar to that above, in the context of the Regulatory Experts' qualifications.

Generally, experts may not offer opinions concerning a legal question. Levin v. Dalva Bros., Inc., 459 F.3d 68, 79 (1st Cir. 2006); Nieves-Villanueva v. Soto-Rivera, 133 F.3d 92, 99 (1st Cir. 1997) ("It is black-letter law that '[i]t is not for witnesses to instruct the jury as to applicable principles of law, but for the judge.'" (alteration in original) (citation omitted)). Moreover, "an expert should not testify to whether a defendant was negligent or to other such matters which 'touch[] on reasonable care, an issue properly left for the jury.'" Peterson, 77 Mass. App. Ct. at 356-357 (alteration in original) (citations and internal quotation omitted); see, e.g., Lind v. Domino's Pizza LLC, 87 Mass. App. Ct. 650, 663-664 (2015) (holding that lower court did not err in permitting plaintiffs' security expert "to testify to his opinion of numerous deficiencies in [defendant's] security plan" and in not allowing him "to provide legal conclusions whether those plans were negligent").

In Massachusetts, regulations are admissible, and it is "a function of the jury to decide whether there was a violation of the [regulation]. . . . [An expert is] properly precluded from giving the jury his opinion interpreting the [regulation] and the effect thereof on facts to be found by the jury." Perry v. Medeiros, 369 Mass. 836, 842 (1976) (citations omitted); cf. Mass. G. Evid. § 414 ("Safety rules, governmental regulations or ordinances, and industry standards may be offered by either party in civil cases as evidence of the appropriate care under the

circumstances."). Similarly, "[e]xpert testimony on industry standards is common fare in civil litigation." Levin, 459 F.3d at 79; see DiMarzo v. American Mut. Ins. Co., 389 Mass. 85, 103 (1983) ("[T]he existence of a custom and usage is a question of fact and may not be proven by opinion."). The expert, however, cannot provide an opinion as to the legal effect of the industry standard. See DiMarzo, 389 Mass. at 103; see, e.g., Nieves-Villanueva, 133 F.3d at 100 n.12 ("[Defendant's expert in governmental personnel matters] was competent to testify that plaintiffs' appointments [of employees] were irregular in the sense that they did not conform to normal personnel practice, but her legal conclusion that the appointments were in violation of the law was improper."); Ji v. Bose Corp., 538 F. Supp. 2d 354, 356, 359 (D. Mass. 2008) (holding that expert could testify to industry practice with respect to contractual releases in modeling industry, but she could not render legal conclusion by "evaluat[ing] the legal effect of each form").

The Regulatory Experts are therefore permitted to identify the industry standards, but they cannot opine as to whether Fresenius breached or violated those industry standards or applicable laws or regulations. See Hearing Transcript (10/15/2015), at 117. Plaintiffs' counsel agreed that Fresenius records speak "for themselves, and [the Regulatory Experts are] just explaining the significance of them in terms of industry standards and industry practice." Hearing Transcript (10/15/2015), at 118.

C. Narration

Finally, Fresenius argues that the court should not permit the Regulatory Experts to "narrate" the Fresenius documents on which they relied in forming their opinions. First, the

Plaintiffs agree that it is "not in [their] best interest to put [the Regulatory Experts] on the stand to drone on and on." Hearing Transcript (10/15/2015), at 111; see, e.g., Hearing Transcript (10/15/2015), at 109-110. Second, the analyses above informs this discussion in that the Regulatory Experts cannot use Fresenius' documents to render opinions of causation that are outside their expertise and they cannot render opinions that constitute legal conclusions. Third, this type of testimony, if it occurs, may be addressed by objections at trial. Just because a disclosure report may be framed in a narrative fashion does not mean that the expert may deliver his or her testimony that way.

PLAINTIFFS' MOTIONS

IV. Plaintiffs' Motion to Preclude Expert Testimony of Ben Lipps

Ben Lipps, Ph.D. ("Dr. Lipps") was the chief executive officer of Fresenius from 1999 through the end of 2012. The Plaintiffs challenge two of Dr. Lipps' opinions, arguing that they are not generally accepted and rest on flawed methodology.

The Plaintiffs challenge Dr. Lipps' opinions that, first, a patient's serum bicarbonate level cannot exceed the bicarbonate prescription, and, second, that the bicarbonate delivered to the patient cannot exceed the bicarbonate prescription entered onto the dialysis machine. These opinions, the Plaintiffs argue, are contrary to the generally accepted principle that the acetate in the dialysate adds to the patient's bicarbonate level. Fresenius conceded at the hearing on this motion, however, that Dr. Lipps would not testify to the effect of the amount of acetate in GranuFlo or NaturaLyte. Hearing Transcript (10/14/2015), at 203-204. Specifically, Fresenius' counsel stated that, as a trial witness, Dr. Lipps would "simply state the facts as he knows them, and that will include the fact of how his dialyzer works, the fact of how diffusion works."

Hearing Transcript (10/14/2015), at 200. The Plaintiffs' argument is therefore moot.

Moreover, Fresenius contends Dr. Lipps did not make the precise comments the Plaintiffs attribute to him. Rather, Dr. Lipps states in his report, "If the serum bicarbonate concentration were to exceed the bicarbonate concentration in the dialysate, it would diffuse back out and come back to the same equilibrium. This is based on basic principles of chemical engineering. In essence, this is what makes hemodialysis work." Dr. Lipps Report (Exhibit 1 to Fresenius' Opposition), at par. 17. Further, "[b]ecause the direction of bicarbonate diffusion would switch at the point when the serum bicarbonate concentration surpasses the dialysate concentration, the post-dialysis serum concentration is effectively controlled by the bicarbonate concentration in the dialysate." Dr. Lipps Report (Exhibit 1 to Fresenius' Opposition), at par. 18; see Dr. Lipps Deposition (Exhibit 25 to Plaintiffs' Motion), at 68-69 (testifying that setting on dialysis machine reflecting bicarbonate prescription is "the highest concentration [the patients are] going to get. They won't come off higher than that"). Fresenius acknowledges that these concepts are debated within the scientific community. See Hearing Transcript (10/14/2015), at 204.

The Plaintiffs' motion is accordingly **DENIED**.

V. Plaintiffs' Motion to Exclude Opinions of Defense Expert Lee Jen Wei

Dr. Lee Jen Wei ("Dr. Wei") is a biostatistician who prepared a report for Fresenius detailing how the statistical analysis in Fresenius' 2010 study is unreliable and the analysis of the results is flawed, and discussing a study Fresenius conducted on its 2010 data ("Flythe Study"). The Plaintiffs seek to exclude three of Dr. Wei's opinions concerning the Flythe Study.

A. First Opinion

In his expert report, Dr. Wei states: "Unlike the Flythe Study, the study design presented

in [Fresenius' 2010 study] was not adequate because it did not use matching to eliminate important differences in nonmodifiable confounders (i.e., age, sex, race, and diabetes status) between [cardiopulmonary arrest] cases and non-[cardiopulmonary arrest] controls." Dr. Wei Report (Exhibit 1 to Plaintiffs' Motion), par. 86 (footnote omitted). The Plaintiffs interpret this language as stating that "matching" is the only accepted methodology and argue that Dr. Wei should be precluded from testifying to that effect because this notion is not generally accepted.

Dr. Wei explained at his deposition that, when conducting a case-control study, the first step is generally matching, "[a]nd then second stage . . . [is] a regression analysis, taking care of the rest of [the] confounding effect." Dr. Wei Deposition (Exhibit 18 to Fresenius' Opposition), at 194. In Fresenius' 2010 study, however, "the team didn't do matching in the first place. They directly us[ed] regression analysis, and ignored the so-called matching technique." Id. He clarified that he "didn't use the word 'must'" when describing the two-step process, he "said [doing matching first is] a most efficient way." Dr. Wei Deposition (Exhibit 18 to Fresenius' Opposition), at 195. An article to which Dr. Wei cited during his deposition as support for his position studied "the utility of matched sampling and regression adjustment . . . for controlling specific matching variables in observational studies." Exhibit 22 to Fresenius' Opposition, at 3. "[M]atched sampling and regression adjustment may be used alone or in combination, that is samples may be random or matched, and regression adjustment may or may not be performed." Id. The result of the study this author conducted led to "[t]he broad conclusion that . . . [matching] coupled with regression adjustment on the matched pairs is a quite effective general plan for controlling the bias due to matching variables, and this combination is clearly superior to regression adjustment on random samples." Id. Further, the study results discussed in the

article "demonstrate[d] quite clearly that matching can dramatically improve estimation." Exhibit 22 to Fresenius' Opposition, at 11.

Dr. Wei is not permitted to testify at trial that the Flythe Study was inadequate because it did not include matching, thus, to this extent, the Plaintiffs' motion is **ALLOWED**. Dr. Wei is, however, permitted to testify that using matching and logical regression together is superior to using logical regression alone. Indeed, at the hearing on this motion, Plaintiffs' counsel responded in the negative to the following question from the court: "[I]f [Dr. Wei's] opinion were limited to the idea that both together are better than one or the other alone, would the opinion be subject to challenge, then?" Hearing Transcript (10/15/2015), at 13; see Hearing Transcript (10/15/15), at 15-16 ("That is a criticism about the way the data was used [and therefore appropriate]. It is not a statement . . . of what is necessary for an appropriate study generically . . . ."). To this extent, then, the Plaintiffs' motion is **DENIED**.

B. Second and Third Opinions

The Plaintiffs seek to preclude Dr. Wei from offering testimony on the first and last sentences of paragraph 89 in his report:

> "*The analyses presented in [Fresenius' 2010 study] did not account for other potential risk factors that are likely to be associated with [cardiopulmonary arrest]*. While purporting to adjust for the influence of confounding factors, the [2010 study] analysis actually considered only a select few laboratory factors (albumin, hemoglobin, phosphorous, calcium, and white-blood-cell count) and vascular access, without considering other factors known to contribute to [cardiopulmonary arrest] and other cardiovascular-related outcomes, such as potassium and calcium levels, body mass index, a history of coronary heart disease or heart failure, normalized protein catabolic rate, and missed treatments. *As the [2010 study] analysis does not attempt to control for the influence of such important confounding factors, and because there may be confounding due to other unobserved factors, it cannot establish whether an independent relationship exists between serum bicarbonate levels and [cardiopulmonary arrest]*."

Dr. Wei Report (Exhibit 1 to Plaintiffs' Motion), par. 89 (footnote omitted). Essentially, Dr. Wei's opinion is that the 2010 study adjusted for some factors, but not other factors "known to contribute to [cardiopulmonary arrest] and other cardiovascular-related outcomes . . . ." Dr. Wei Report (Exhibit 1 to Plaintiffs' Motion), par. 89. Failure to account for these "important confounding factors," Dr. Wei opines, prevents the 2010 study from establishing "an independent relationship between serum bicarbonate levels and [cardiopulmonary arrest]." Id.

The Plaintiffs argue that these opinions are speculative and should be excluded because Dr. Wei himself did not determine the confounders for which adjustment would have been appropriate. See Dr. Wei Deposition (Exhibit 13 to Plaintiffs' Motion), at 204. Moreover, reliance on the Flythe Study to demonstrate that the results changed when such confounder adjustments were made is misleading because the 2010 study and Flythe Study are too different to compare.

The court disagrees that Dr. Wei's opinions should be excluded. Dr. Wei's reliance on the Flythe Study, or any other study, to demonstrate the shortcomings of the 2010 study goes to the weight of his opinion and is a subject for cross-examination. The Plaintiffs' challenge to Dr. Wei's competence to opine on confounders because he is admittedly not a clinician also fails for this reason as well as for the fact that he relied on the studies of other clinicians to "fill[] in the gap of his not being" a clinician. See Hearing Transcript (10/15/2015), at 28-32 (discussing studies on which Dr. Wei relied).

The Plaintiffs' motion to exclude Dr. Wei's testimony on this basis is accordingly **DENIED**.

VI. **Plaintiffs' Motion to Preclude Opinions of Defense Expert Dr. Glenn Chertow**

At the hearing on this motion, Fresenius agreed to "withdraw Dr. Chertow as a general causation expert for anything other than, if it's even necessary, teaching the jury the fundamental principles behind how the kidney functions and how dialysis works and offer no additional opinions." Hearing Transcript (10/15/2015), at 45. The court therefore takes no action on the Plaintiffs' motion.

VII. **Plaintiffs' Motion to Preclude the Expert Testimony of Dr. Franklin Maddux**

Dr. Franklin Maddux ("Dr. Maddux") is Fresenius' current chief medical officer. He produced three separate expert reports: the Opening Expert Report (Exhibit 19 to Plaintiffs' Motion); the Rebuttal Expert Report (Exhibit 20 to Plaintiffs' Motion); and the First Supplemental Rebuttal Expert Report (Exhibit 18 to Plaintiffs' Motion). Fresenius intends to call Dr. Maddux as a witness to present the data that he asked Dr. Norma Ofsthun to compile concerning the yearly mean pre-dialysis and post-dialysis serum bicarbonate level for Fresenius patients,[7] and to opine that the data is inconsistent with the Plaintiffs' theory. See Hearing Transcript (10/15/2015), 77, 79, 80; see also Dr. Norma Ofsthun Report (Exhibit 5 to Fresenius' Opposition).

A. First Opinion

In his Rebuttal Expert Report, Dr. Maddux opines, "Plaintiffs' experts have put forth no medical evidence, nor am I aware of any medical evidence, of any 'general causation' between

[7]The Plaintiffs do not dispute that Dr. Maddux can present the data as a fact witness. Hearing Transcript (10/15/2015), at 81.

use of NaturaLyte or GranuFlo and adverse cardiac events suffered by hemodialysis patients treated with those products." Dr. Maddux Rebuttal Expert Report (Exhibit 20 to Plaintiffs' Motion), par. 42. The Plaintiffs argue that the court should preclude Dr. Maddux from testifying to this effect because he did not consider all of the literature that the Plaintiffs' experts considered, and because the evidence he did consider is anecdotal evidence that Fresenius prepared in anticipation of litigation. See Hearing Transcript (10/15/2015), at 68 ("[T]he core of what [the Plaintiffs] are saying in terms of competence . . . is that [Dr. Maddux] just has not done enough work in this area himself to be able to opine meaningfully about it."); Hearing Transcript (10/15/2015), at 70 (arguing that Dr. Maddux "has done far less rigor or research in this area historically in his own professional career [than other experts involved in this case], almost none, and . . . as a matter of qualifications and of methodology, Dr. Maddux ought to be struck from offering any expert opinions in this case").

While generally, failure to consider all the available literature would affect the probativeness of an opinion rather than its admissibility, see Salvas, 452 Mass. at 360, Dr. Maddux does not appear to have considered *any* lines of evidence supporting the Plaintiffs' theory. See Plaintiffs' Motion, at 12 & nn.45-50. Dr. Maddux is therefore precluded from opining at trial that there is "no medical evidence" to support the Plaintiffs' theory of general causation. The Plaintiffs' motion on this point is accordingly **ALLOWED**.

B. Second Opinion

The Plaintiffs argue that Dr. Maddux mischaracterizes the Plaintiffs' position regarding total buffer, thus his rebuttal opinions based on those mischaracterizations should be excluded.

Dr. Maddux Opening Expert Report, par. 13. Dr. Maddux, they argue, misconstrues the Plaintiffs' total buffer theory as "specific arithmetic" meaning that a bicarbonate concentrate prescription of 35 mEq/L plus GranuFlo, i.e., 8 mEq/L of acetate, results in a "total buffer" of 43 mEq/L of bicarbonate. See Dr. Maddux Opening Expert Report, pars. 13, 43. The thrust of the parties' underlying dispute, as Plaintiffs' counsel described it, is how much acetate ends up in the blood as bicarbonate. Hearing Transcript (10/15/2015), at 54. Fresenius "never looked at the answer of what [its] product actually does. . . . until . . . the ABChD Study." Id. Further, even accepting Fresenius' position that the process of diffusion will prevent a patient's post-dialysis serum bicarbonate from significantly exceeding the bicarbonate concentrate prescription, the Plaintiffs are concerned with the clinical effect "when [the increase in bicarbonate that results from the liver's metabolizing the acetate] is happening . . . ." Hearing Transcript (10/15/2015), at 55.

As Fresenius points out, however, the Plaintiffs' Amended Master Complaint defines "total buffer level" as "the sum of the bicarbonate from the base and the bicarbonate converted from the acetate in the acid portion fo the dialysate. Thus, if there are 33 mEq/L of bicarbonate from the bicarbonate concentrate and 4 mEq/L of acetate from the acid concentrate, the total buffer level is 37 mEq/L." Amended Master Complaint, par. 88.[8] Moreover, any error in Dr. Maddux's testimony goes to the weight of that testimony and can be addressed on cross-examination. See, e.g., Sullivan v. First Mass. Fin. Corp., 409 Mass. 783, 791-792 (holding that, where plaintiffs' experts based their testimony on "at least two assumptions that were not

[8]More accurately, Fresenius cites to the Plaintiffs' original complaint, which has an identical allegation at paragraph 110.

factually correct[,]" defendants brought error to jury's attention through cross-examination, and "errors went to the weight of that testimony").

The Plaintiffs' motion to preclude Dr. Maddux from characterizing the Plaintiffs' total buffer theory in this way is therefore **DENIED**.

C. Alternative Argument

Finally, the Plaintiffs argue that Dr. Maddux's expert testimony may imbue his fact testimony with more credibility than the testimony of other witnesses. Therefore, they alternatively argue that the court exclude Dr. Maddux's testimony pursuant to Mass. G. Evid. § 403, which permits the court to "exclude relevant evidence if its probative value is substantially outweighed by a danger of one or more of the following: unfair prejudice, confusing the issues, misleading the jury, undue delay, wasting time, or needlessly presenting cumulative evidence." Notwithstanding Fresenius' argument that this request is outside the scope of a Daubert-Lanigan motion, the Plaintiffs' argument fails at this time. See generally Note to Mass. G. Evid. § 403; see, e.g., Ji, 538 F. Supp. 2d at 358-359 (rejecting plaintiff's argument that, even if defendant's witness qualifies as an expert the court should exclude her because "the jury will be confused and possibly unduly influenced by [her] dual role as a fact witness and also an expert[,]" and holding that "the roles of fact witness and expert witness are not necessarily mutually exclusive and . . . [plaintiff] has not substantiated her allegation that [witness'] testimony will be unfairly prejudicial").

VIII. **Plaintiffs' Motion to Exclude Expert Testimony of Jeffrey N. Gibbs, Esq.**

Fresenius expects Jeffrey N. Gibbs, Esq. ("Gibbs") to testify at trial on the standard of care or design controls required for GranuFlo and NaturaLyte. The Plaintiffs seek to exclude his

opinion that Fresenius was not required to follow the design control standards for these products because the labeling changes to the products did not constitute "changes" within the scope of the FDA's Quality System Regulation.

The FDA's Quality System Regulation ("QSR"), 21 C.F.R. § 820 et seq., "is intended to be a flexible, framework regulation. . . . provid[ing] general requirements that a medical device manufacturer must implement as applicable and to the appropriate extent based on the risk posed by the devices being manufactured. Device companies have considerable latitude in deciding how to implement these provisions." Gibbs Report (Exhibit 1 to Fresenius' Opposition), par. 71. The QSR requires "that manufacturers establish procedures so that, among other things, personnel with management responsibility review and assess the quality system, document and purchasing controls, and records regarding device specifications and processing." Gibbs Report (Exhibit 1 to Fresenius' Opposition), par. 72. In 1996, the "FDA established a design control requirement for all Class II and Class III devices. . . . There is no reference to design controls in the certification provided by an applicant in a 510(k)." Gibbs Report (Exhibit 1 to Fresenius' Opposition), par. 73 (citations omitted). The FDA

> "explained in the preamble to the final regulation that the [FDA] 'did not intend the design requirements to be retroactive,' and the design control section of the QSR regulation '[did] not require a manufacturer to apply such requirements to already distributed devices.' . . . [Rather,] the design control requirements would apply 'to designs that are in the design and development phase, and manufacturers of such designs will be expected to have the design and development plan established.' . . . Thus, the design control requirements would not apply to devices designed earlier. . . . only to designs that were in the development stage on or after June 1, 1997, and to modifications that occurred after June 1, 1997."

Gibbs Report (Exhibit 1 to Fresenius' Opposition), par. 74 (alteration in original) (internal

citations omitted);[9] see Gibbs Report (Exhibit 1 to Fresenius' Opposition), par. 75 (discussing "corrective and preventive action" provision of QSR). Gibbs concluded that,

> "[b]ecause both GranuFlo and NaturaLyte were cleared prior to the design control provision, [Fresenius] was not obligated to implement design controls at the time they were cleared or subsequently. *The subsequent clearances that occurred after the design control provision took effect were for changes in manufacturing, not changes to design, and thus those modifications did not involve design controls*."

Gibbs Report (Exhibit 1 to Fresenius' Opposition), par. 74 (emphasis added); see Gibbs Deposition (Exhibit 2 to Plaintiffs' Motion), at 227-229 (testifying that he looked at 510(k) summaries, but not full submissions); Gibbs Deposition (Exhibit 2 to Plaintiffs' Motion), at 237 ("You can change the manufacturing process and not change the resulting product."); Gibbs Deposition (Exhibit 2 to Plaintiffs' Motion), at 245-248 (testifying that changes to product's labeling are not change to product's design); Gibbs Deposition (Exhibit 2 to Plaintiffs' Motion), at 351-352 (looking at Fresenius' 2007 510(k) submission summary and opining that product's "minor changes" did not bring product within design control regulations because "[t]echnological characteristics are the same").

The actual guidance from the FDA on this portion of the QSR, as set forth in the Federal Register, however, states:

> "FDA disagrees with the comments that suggest that the design output should be restricted to physical characteristics of the device. *Design output includes, among other things, the specification for the manufacturing process, the quality assurance testing, and the device labeling and packaging.* It is important to note that the design effort should not only control the design aspects of the device during the original development phase, but all subsequent design and development activities including any redesign or design changes after the original design is transferred to production."

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[9]The Plaintiffs do not dispute Gibbs' interpretation of the QSR insofar as it concerns "grandfathering," described here. Hearing Transcript (10/15/2015), at 130.

61 Fed. Reg. 52,233, 52,608 (1996) (emphasis added).

Given that the FDA itself does not recognize Gibbs' interpretation of the QSR, Gibbs cannot testify that changes in a product's labeling or packaging do not constitute design changes triggering the requirements under the QSR.[10] On this basis, therefore, the Plaintiffs' motion is **ALLOWED**.

IX. **Plaintiffs' Motion to Exclude Opinions of Marc Shalek, M.D.**

Fresenius retained cardiologist Dr. Marc Shalek ("Dr. Shalek") "to review, study, analyze the evidence in this case and provide expert opinion testimony regarding whether there is a causal relationship between the use of Granuflo [sic] and Naturalyte [sic] in hemodialysis . . . therapy and sudden cardiac arrest . . ., sudden cardiac death . . ., or other cardiac events in patients with end stage regnal disease undergoing [hemodialysis] therapy." Dr. Shalek Rebuttal Expert Report (Exhibit 1 to Fresenius' Motion), par. 1. "Specifically, [he] has been asked to review the reports from Plaintiffs' expert witnesses, including Drs. Julian M. Aroesty, Joseph Shawn Miles, Arthur Z. Schwartzbard, and Douglas P. Zipes, . . . and provide responsive observations and opinions." Id. Based on this review, Dr. Shalek opines that there is no causal relationship between the use of GranuFlo or NaturaLyte and sudden cardiac arrest, sudden cardiac death, or any other cardiac event, and there is no evidence that the acetate from GranuFlo or NaturaLyte "that was diffused into a patient's blood during dialysis" caused sudden cardiac death "hours after dialysis." Dr. Shalek Rebuttal Expert Report, pars. 3-4. To render these opinions, Dr. Shalek reviewed the reports of the Plaintiffs' experts he was retained to rebut,

[10]Fresenius' counsel essentially conceded this point at the hearing on this motion. See Hearing Transcript (10/15/2015), at 129.

including "data, studies, publications, deposition testimony, and other materials . . . ." Dr. Shalek Rebuttal Expert Report, par. 10; see Dr. Shalek Rebuttal Expert Report, Exhibit B (listing materials he reviewed).

The Plaintiffs seek to exclude Dr. Shalek's testimony because he did not take into consideration the evidence that the Plaintiffs' experts relied on when rendering his opinions and he did no independent research. As Fresenius points out, however, the methodology Dr. Shalek employed was that of a rebuttal expert. "'The function of rebuttal testimony is to explain, repel, counteract or disprove evidence of the adverse party.'" Aviva Sports, Inc. v. Fingerhut Direct Mktg., Inc., 829 F. Supp. 2d 809, 834 (D. Minn. 2011). This court finds persuasive the general notion that

> "[i]t is the proper role of rebuttal experts to critique plaintiffs' expert's methodologies and point out potential flaws in the plaintiff's experts' reports. . . . [and that by] appl[ying] their expertise to the facts and methodologies used by each of [the opposing side's] experts in forming their conclusions[,] . . . . [the rebuttal experts'] testimony is not unduly speculative. . . . [but] will be helpful for the jury to weigh the evidence presented at trial."

Id. at 835. Further, any failure by Dr. Shalek in considering all of the Plaintiffs' experts' materials goes to the weight of his testimony, not its admissibility. See Salvas, 452 Mass. at 360.

The Plaintiffs' motion to exclude Dr. Shalek's testimony is accordingly **DENIED**.

X. Plaintiffs' Motion to Exclude the Expert Testimony of James J. Zazra, Ph.D.

Microbiologist James J. Zazra, Ph.D. ("Dr. Zazra") is the general manager of Spectra Clinical Research ("Spectra"), a Fresenius-owned company, which "is a global provider of central laboratory services that supports clinical trials of all sizes, including trials conducted by medical device companies in connection with their FDA registrations." Dr. Zazra Expert Report (Exhibit 4 to Plaintiffs' Motion), par. 9; see Dr. Zazra Expert Report (Exhibit 4 to Plaintiffs'

Motion), par. 11 (explaining that "[m]any, if not most, dialysis clinics send patients' [blood] samples off-site for analysis at centralized labs, such as Spectra, that specialize in the unique handling, testing, and reporting requirements of the dialysis patient population"). Fresenius asked Dr. Zazra to "focus on: (1) variables that can affect patient serum bicarbonate values reported by a reference laboratory, and (2) the accuracy of serum bicarbonate values reported by Spectra . . . ." Dr. Zazra Expert Report (Exhibit 4 to Plaintiffs' Motion), par. 1.[11] Based on his experience and the materials he reviewed, Dr. Zazra rendered the following two opinions:

> 1. "The most important pre-analytical variables for serum bicarbonate values are the practices and workflows of the laboratory conducting the measurement, particularly the amount of time the serum is exposed to the air before the serum bicarbonate value is measured. The analytical method used to measure the serum bicarbonate level also may have a statistically significant effect on the results. Shipping blood samples by air, in contrast, has no effect on serum bicarbonate values when samples are analyzed using identical instrumentation and workflows." Dr. Zazra Expert Report (Exhibit 4 to Plaintiffs' Motion), par. 10
>
> 2. "Spectra . . . has implemented effective measures to reduce the time serum is exposed to the air in the samples it analyzes, thereby protecting the integrity of samples and preserving the bicarbonate results." Id.

The Plaintiffs seek to exclude Dr. Zazra's testimony because he bases his opinion that Spectra's bicarbonate readings are accurate on his own 2000 study, and because he failed to consider other factors that can affect the accuracy of bicarbonate readings.[12]

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[11]Fresenius also asked Dr. Zazra "to review and comment on certain opinions expressed in the expert reports of B. Burt Gerstman, Ph.D., and Sushrut S. Waikar, MD, MPH, offered on behalf of [P]laintiffs." Dr. Zazra Rebuttal Expert Report (Exhibit 5 to Plaintiffs' Motion), par. 2.

[12]Interestingly, as Fresenius points out, the Plaintiffs' expert, Dr. Derek Fine, writes in his expert report concerning a different plaintiff that "[Fresenius] and Spectra laboratories have tremendous experience in processing numerous blood samples by standardized methods and therefore the bicarbonate levels are likely to be accurate . . . ." Dr. Derek Fine Report (Exhibit 1 to Fresenius' Opposition), at 7.

In 2000, Dr. Zazra, along with Shelden Rosenblum, M.S., published an article titled "The Effect of Pre-Analytical Variables on Serum Bicarbonate (total CO_2) Values" ("2000 Article") that discussed the results of a study ("2000 Study") they conducted at Spectra's laboratories that:

> "(1) compared serum bicarbonate measurements obtained for samples from healthy volunteers (employees) at Spectra's facilities in New Jersey and Southern California that were tested both locally and across the country; (2) examined [Spectra's] laboratory data files pertaining to patient samples that had been transported by ground or by air; (3) analyzed the results of the . . . initiative within Spectra to reduce the time specimens spent waiting for analysis in open autoanalyzer cups; and (4) analyzed survey data from the College of American Pathologists regarding different methods for measuring total CO_2."

Dr. Zazra Expert Report (Exhibit 4 to Plaintiffs' Motion), par. 13; see 2000 Article (Exhibit 10 to Plaintiffs' Motion). As a result of the study, Dr. Zazra and his co-author concluded:

> "Our data clearly demonstrate that when comparisons are carried out either within a single laboratory or between laboratories that use identical instruments and work flows, *the mode by which specimens reach the laboratory has no effect on the results*. Other studies, both published and not, that have addressed this issue are confounded by differences between laboratory instruments and the way laboratories work.
>
> . . . .
>
> ". . . . Dialysis clinics that send patient samples to distant laboratories do not need to be concerned about the effect of that shipping on the results.
>
> "Laboratories serving [end stage renal disease] patients must examine their practices and work flows to ensure that every effort is made to preserve the bicarbonate results."

2000 Article (Exhibit 10 to Plaintiffs' Motion), at 4 (emphasis added); see Dr. Zazra Expert Report (Exhibit 4 to Plaintiffs' Motion), par. 13 (listing conclusions reached from study). Basically, then, the results from the 2000 Study led Dr. Zazra to conclude that shipment of blood samples from the clinic to the laboratory does not impact the bicarbonate levels in the samples. See id.

First, the Plaintiffs argue that Dr. Zazra cannot rely on the 2000 Article because it was not peer reviewed, which Dr. Zazra himself concedes. Dr. Zazra Deposition (Exhibit 3 to Plaintiffs' Motion), at 48 ("[T]his article was not peer reviewed . . . ."). Peer review is "a relevant, though not dispositive, consideration in assessing the scientific validity of a particular technique or methodology on which an opinion is premised[,]" Daubert, 509 U.S. at 594, because "submission to the scrutiny of the scientific community is a component of 'good science,' in part because it increases the likelihood that substantive flaws in methodology will be detected." Id. at 593. As Fresenius points out, however, the 2000 Article was published, and the scientific community did scrutinize it. E.g., Letters to the Editor Regarding the 2000 Article (Exhibit 7 to Plaintiffs' Motion). This argument therefore fails.

Second, the Plaintiffs argue that the 2000 Study used equipment that is now obsolete, and Dr. Zazra has not attempted to replicate the results from the 2000 Study with his current equipment, thus the 2000 Study reflects what was known in 2000, not today. Dr. Zazra testified at his deposition, however, that the equipment used in 2000 and the equipment used today "give very similar results." Dr. Zazra Deposition (Exhibit 3 to Plaintiffs' Motion), at 85. Moreover, this challenge goes to the weight of Dr. Zazra's testimony rather than its admissibility.

Third, the Plaintiffs argue that in the 2000 Study, Dr. Zazra focused only on differences in delay and transportation, and in his Expert Report, he did not consider other factors outside Spectra's control that could impact the bicarbonate results, thereby rendering his opinion as to the accuracy of the Spectra lab results unreliable. "'Normally, failure to include variables will affect that analysis' probativeness, not its admissibility.'" Salvas, 452 Mass. at 360 (citation omitted). This challenge, therefore, goes to the weight of Dr. Zazra's testimony rather than its

admissibility.

The Plaintiffs' motion is accordingly **DENIED**.

FRESENIUS' MOTION ON SPECIFIC CAUSATION

I. Fresenius' Motion to Exclude Expert Testimony of Dr. David S. Goldfarb and Dr. Julian M. Aroesty

Plaintiffs' specific causation experts, nephrologists Dr. David Goldfarb ("Dr. Goldfarb") and Dr. Julian M. Aroesty ("Dr. Aroesty"), concluded that GranuFlo was a significant contributing factor in the decedent's death by delivering excess bicarbonate. Fresenius seeks to exclude Dr. Goldfarb's and Dr. Aroesty's specific causation testimony, arguing that they base their reports on the scientifically unreliable Hakim Memo, discussed above, specifically the finding that GranuFlo causes alkalosis by delivering excess bicarbonate to the patient. The Plaintiffs oppose this motion, arguing that Dr. Goldfarb and Dr. Aroesty utilized a differential diagnosis methodology to reach their conclusion that GranuFlo was a substantial contributing factor in the decedent's sudden cardiac arrest. See Dr. Goldfarb Report (Exhibit 1 to Plaintiffs' Opposition), at par. 8 (explaining his use of differential diagnosis in decedent's case); Dr. Aroesty Report (Exhibit 9 to Fresenius' Motion), at 7 ("In arriving at [his] opinion that GranuFlo was a substantial contributing factor in causing alkalosis and the subsequent death of [the decedent], [he] employed the method of differential diagnosis . . . .").

Differential diagnosis "'is a standard scientific technique of identifying the cause of a medical problem by eliminating the likely causes until the most probable one is isolated.'" Hicks's Case, 62 Mass. App. Ct. 755, 761 (2005) (citation omitted). This technique "'has widespread acceptance in the medical community,'" and is "'typically performed after physical examinations, the taking of medical histories, and the review of clinical tests, including

laboratory tests . . . .'" Id. (citations and internal quotation omitted) (ellipses in original).

Dr. Goldfarb writes in his report that he "was asked to review the case of [the decedent] in order to render an opinion regarding his cause of death and to determine if his exposure to GranuFlo, a source of excessive bicarbonate and potential base, was more likely than not an important contributing factor." Dr. Goldfarb Report (Exhibit 1 to Plaintiffs' Opposition), at par. 1. He "extensively reviewed his medical records, the depositions of the physicians involved in his case, the general reports submitted by the [P]laintiffs and [Fresenius] and the relevant medical literature." Id. Similarly, Dr. Aroesty writes in his report that he was asked to review the decedent's case and "determine, whether to a reasonable degree of medical certainty, it is more likely than not, but for the introduction of GranuFlo, [the decedent] would not have died from sudden cardiac arrest caused by an unsafe level of bicarbonate." Dr. Aroesty Report (Exhibit 9 to Fresenius' Motion), at 1. He "reviewed the general causation expert reports of Plaintiffs and [Fresenius] as well as all of [the decedent's] medical records, the testimony and depositions taken of the parties specific to [the decedent's] case including his physicians, as well as the available medical literature." Id.

By starting with the improper premise that GranuFlo is a source of excessive bicarbonate, Fresenius argues, Dr. Goldfarb and Dr. Aroesty did not perform a differential diagnosis. Starting with this improper preconceived notion, Fresenius asserts, renders their opinions inadmissible. In fact, the Plaintiffs argue, this premise is not improper or incorrect, but, rather, is based on sources other than the Hakim Memo. See Plaintiffs' Opposition, at 9-12. The question of whether GranuFlo actually does deliver excess bicarbonate to the patient – and, it follows, to this decedent – is one of fact for the jury to resolve.

Fresenius' motion is accordingly **DENIED**.

PLAINTIFFS' MOTION ON SPECIFIC CAUSATION

I. Plaintiffs' Motion to Exclude Expert Testimony of Herbert Y. Lin, M.D.

Dr. Herbert Y. Lin ("Dr. Lin") is a nephrologist who "review[ed], stud[ied], and analyze[d] the evidence in this case relating to the treatment, medical history, and death of . . . [the decedent] and to provide expert opinions and testimony regarding the likely cause of [the decedent's] death." Dr. Lin Report (Exhibit 4 to Fresenius' Opposition), par. 1. Fresenius also asked Dr. Lin to offer an expert opinion to rebut Dr. Goldfarb's expert report. Dr. Lin Rebuttal Report (Exhibit 1 to Fresenius' Opposition), par. 1. Dr. Lin opines that the decedent's "death was caused by a sudden cardiac event due to his significant medical history and high number of comorbidities. [The decedent's] death was not caused by his dialysis treatment or the use of GranuFlo or NaturaLyte, as there is no evidence demonstrating any potassium or bicarbonate concerns during his time on dialysis." Dr. Lin Report (Exhibit 4 to Fresenius' Opposition), par. 35; see Dr. Lin Rebuttal Report (Exhibit 1 to Fresenius' Opposition), par. 11 (opining that "a much more likely cause [of the decedent's death] is the progression of the other diseases that [the decedent] had. The hemodialysis treatments kept him alive long enough to let his other disease processes naturally progress until they caused his death").

The Plaintiffs seek to exclude Dr. Lin's testimony because Dr. Lin did not include GranuFlo – more specifically, the alkalosis and hypokalemia caused by GranuFlo's delivery of excess bicarbonate – as a possible cause of the decedent's death, thereby rendering his differential diagnosis unreliable. In his deposition, in response to the question, "Is it possible for someone to have a cardiac arrhythmia as a result of becoming hypokalemic?" Dr Lin responded,

in pertinent part, "[F]rankly I don't know[,]" he had never seen a patient experience cardiac arrest as a result of hypokalemia during his years of practice, and he did not review any "cardiology textbooks in preparation of either of [his] reports[.]" Dr. Lin Deposition (Exhibit 5 to Fresenius' Opposition), at 79-81.

As Fresenius points out, however, Dr. Lin is not a cardiologist; his role is to opine on the nephrology aspect of the decedent's case, and he reviewed the decedent's medical records from that perspective. Further, Dr. Lin did rule out GranuFlo as the cause of the decedent's death based on the fact that "there is no evidence demonstrating any potassium or bicarbonate concerns during his time on dialysis. In fact, [the decedent's] [potassium] and serum bicarbonate were remarkably stable throughout his time on dialysis." Dr. Lin Report (Exhibit 4 to Fresenius' Opposition), par. 35. Further, he opined that "[t]he dialysis treatments were actually keeping [the decedent] alive from the time he started dialysis until his death . . . ." Dr. Lin Report (Exhibit 4 to Fresenius' Opposition), par. 36. As he explained at his deposition, "How could something which he had tolerated safely by the records showing that his blood levels of bicarbonate and potassium were fine, how could something which did not change which had kept him alive, so his other diseases could progress, how could something like that be responsible for his demise? So [i.e., GranuFlo] is something which you can exclude [as the cause of his death]." Dr. Lin Deposition (Exhibit 5 to Fresenius' Opposition), at 91.

Dr. Lin's opinion is reliable, and the Plaintiffs' motion is **DENIED**.

ORDER

For the foregoing reasons, the court **ORDERS** that:

- Fresenius' Motion to Exclude Certain Statements in the Hakim Memo as Well as Plaintiffs' Experts' Opinions Based on those Statements is **ALLOWED**;

- Fresenius' Motion to Limit the Opinions and Testimony of Dr. Steven Borkan is **ALLOWED** insofar as it concerns testimony to the effect that an amount of acetate over 2.4 mEq/L is "excess," otherwise it is **DENIED**;

- Fresenius' Motion to Limit the Opinions and Testimony of Plaintiffs' Four FDA Regulatory Experts is **ALLOWED** insofar as the Regulatory Experts' testimony concerns risks created by Fresenius' actions or inactions, and insofar as their testimony concerns breaches or violations of industry standards or regulations, otherwise it is **DENIED**;

- Plaintiffs' Motion to Preclude Expert Testimony of Ben Lipps is **DENIED**;

- Plaintiffs' Motion to Exclude Opinions of Defense Expert Lee Jen Wei is **ALLOWED** insofar as his testimony concerns the inadequacy of the Flythe Study based on the failure to include matching, otherwise it is **DENIED**;

- Plaintiffs' Motion to Preclude the Expert Testimony of Dr. Franklin Maddux is **ALLOWED** to the extent of his testimony that there is "no medical evidence" to support the Plaintiffs' general causation theory, otherwise it is **DENIED**;

- Plaintiffs' Motion to Exclude Expert Testimony of Jeffrey N. Gibbs, Esq. is **ALLOWED**;

- Plaintiffs' Motion to Exclude Opinions of Marc Shalek, M.D., is **DENIED**;

- Plaintiffs' Motion to Exclude the Expert Testimony of James J. Zazra, Ph.D., is **DENIED**;

- Fresenius' Motion to Exclude Expert Testimony of Dr. David S. Goldfarb and Dr. Julian M. Aroesty is **DENIED**;

- Plaintiffs' Motion to Exclude Expert Testimony of Herbert Y. Lin, M.D., is **DENIED**.

Finally, the court takes no action on the Plaintiffs' Motion to Preclude Opinions of Defense Expert Dr. Glenn Chertow[13].

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[13]The court has not taken under advisement the Defendants' Motion to Exclude Expert Testimony of Dr. Clark Colton and Dr. Andrew Zydney, as it has scheduled a further hearing on the matter.

SO ORDERED.

Dated: November 16, 2015

Maynard M. Kirpalani
Justice of the Superior Court